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**Modeling the Effects of Fentanyl and Narcan on the Opioid Epidemic in Allegheny County
Using Mathematics**

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1 Introduction

Opioids are a class of drugs that are widely used to relieve pain and include Morphine, Codeine, and Oxycodone. In the early 1990s, physicians across the U.S. started prescribing opioids at an increased rate [1]. Since then, both prescription and illicit opioid use has fueled an epidemic and resulted in a high number of overdose deaths. In 2017, the number of opioid overdose fatalities peaked, and the U.S. declared a public health emergency [2]. One state in particular that has contributed significantly to this epidemic is Pennsylvania, which ranks first for the greatest number of overdose deaths and third for the highest death rate [1]. In fact, Allegheny County has witnessed an overdose death rate that is three times that of the national average [3].

Between 2015-2017, the number of drug overdose deaths increased dramatically in Pennsylvania due in part to the synthetic opioid, fentanyl [4]. Fentanyl is easier to produce and more difficult to regulate because it is distributed from foreign countries [4]. Since it is 80-100 times more powerful than morphine, addicts and dealers often mix it with other opioids to increase their potency and users are more likely to suffer from an overdose [5].

Naloxone (commonly known by its brand name Narcan) is medication used to block the effects of opioids [6]. In 2017, Governor Tom Wolf increased state funding to combat the opioid epidemic, allocating \$5 million for Narcan [7]. As a result, the number of prescriptions for Narcan doubled and Allegheny County experienced a sharp decline in overdose deaths [1].

This study aims to quantify the effects that fentanyl and Narcan have had on the opioid epidemic in Allegheny County and analyze the extent to which an increase in the availability of Narcan can decrease overdose fatalities. For this project, we collaborated with Peter Jhon, a data analyst from the Allegheny County Department of Human Services, to develop a mathematical model of the opioid epidemic and analyze model output related to our research goals.

2 Model Description

Our mathematical model describes the relationships between four population classes—Susceptible (S), Prescribed (P), Addicted (A), and Recovered (R)—and how the size of each changes over time. The S class represents the proportion of the population that is not using opioids nor actively recovering from addiction while the P class is the proportion that is currently using opioids as prescribed. The A class represents the proportion of the population that is addicted to opioids, and the R class represents the proportion that is in treatment for addiction.

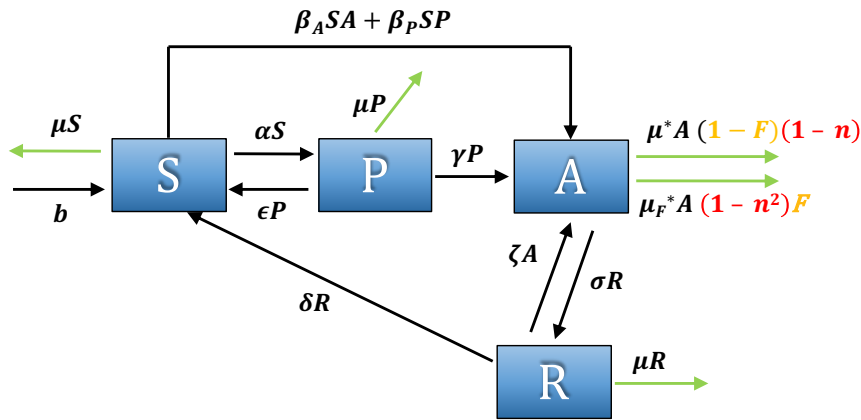


Figure 1. Diagram of mathematical model describing the opioid epidemic.

A schematic of the model is illustrated in Figure 1 where the arrows indicate the movement into and out of each class. Green arrows represent death, which can occur at a natural rate (μ) or at increased rates due to addiction (μ^* , μ_F^*). Parameters describing the percentage of drugs with fentanyl (F) and the availability of Narcan (n) are included. Narcan reduces the death rate of addicts ($1 - n$); however, it is less effective when fentanyl is present ($1 - n^2$). The model is expressed mathematically as the following system of differential equations.

$$\frac{dS}{dt} = -\mu S - \alpha S - \beta_A SA - \beta_P SP + \delta R + \epsilon P + b \quad (1)$$

$$\frac{dP}{dt} = \alpha S - \epsilon P - \gamma P - \mu \quad (2)$$

$$\frac{dA}{dt} = -\zeta A - \mu^* A (1 - F)(1 - n) - \mu_F^* A (1 - n^2) F + \gamma P + \alpha R + \beta_A SA + \beta_P SP \quad (3)$$

$$\frac{dR}{dt} = -\sigma R - \mu R - R + \zeta A \quad (4)$$

3 Parameters and Simulations

Table 1 shows the values of the parameters used in all model simulations. The parameters highlighted in orange represent local rates and were estimated using data provided by the Allegheny County DHS or obtained from U.S. Census data [8, 9]. All other values represent national averages obtained from a model of the U.S. opioid epidemic [10]. Values of F and n range from 0 to 1.0 and varied in our simulations in order to determine their impact on model output.

Table 1: Values of parameters used in model simulations. All values represent yearly rates. Parameters highlighted in orange indicate values specific to Allegheny County.

Notation	Description	Value	Source
α	Prescription rate per person per year	0.15	CDC (2017)
ϵ	End prescription without addiction (rate)	1.0	Shah et al. (2017)
β_P	Illicit addiction rate based on P -class	0.021812	Allegheny County DHS, Han et al. (2017), Hughes et al. (2017)
β_A	Illicit addiction rate based on A -class	0.007708	Allegheny County DHS, Han et al. (2017), Hughes et al. (2017)
γ	Prescription-induced addiction rate	0.00744	Vowles et al. (2015), Shah et al. (2017)
ζ	Rate of entry into rehabilitation	1.00	Battista et al. (2019)
σ	Natural relapse rate of R -class	0.9	Smyth et al. (2010), Bailey et al. (2013)
δ	Successful treatment rate	0.1	Weiss and Rao (2017)
μ	Natural death rate	0.01095	U.S. Census data [8, 9]
μ_F^*	Death rate of addicts using opioids with fentanyl	0.045266	Allegheny County DHS
μ^*	Death rate of addicts using opioids without fentanyl	0.01741	U.S. Census data [8, 9]
F	Percent of opioid drugs containing fentanyl	0 – 1.0	Allegheny County DHS
n	Availability and distribution of Narcan within the community	0 – 1.0	Allegheny County DHS

Equations (1) – (4) were solved numerically and results were graphed using the statistical software R [11]. The package deSolve [12] was used to solve the differential equations.

4 Results

4.1 Optimal values of Fentanyl and Narcan parameters

Model output was used to predict the annual overdose death rate in Allegheny County from 2004 to 2018 for different values of F and n . As seen in Figure 2, model predictions best matched the observed death rate when we assumed 47% of opioid-related addictions involved fentanyl ($F = 0.47$) and Narcan availability increased from $n = 0$ to $n = 0.57$ starting in 2017.

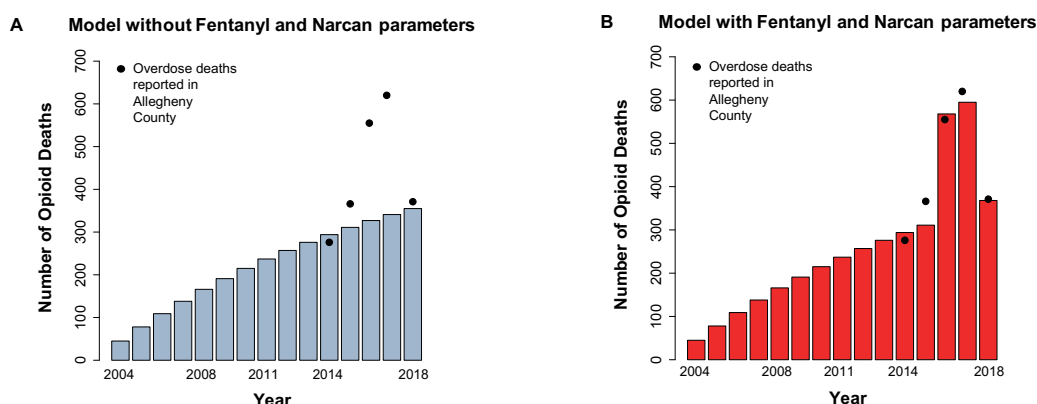


Figure 2: Bar plots show model predictions of the annual number of opioid overdose deaths when (A) the effects of fentanyl and Narcan are ignored ($F = 0, n = 0$); (B) percent of drugs involving fentanyl is increased to 47% in 2015 ($F = 0.47$) and the impact of Narcan is increased from $n = 0$ to $n = 0.57$ in 2017.

4.2 Long-term impact of increasing use of Fentanyl

Model simulations were performed to predict the cumulative number of opioid overdose deaths in Allegheny County over the next decade (2018 – 2028) for different values of F and n . Results in Figure 3 show that as the percentage of drugs containing fentanyl (F) increases, the impact of increasing the availability and distribution of Narcan within the community diminishes.

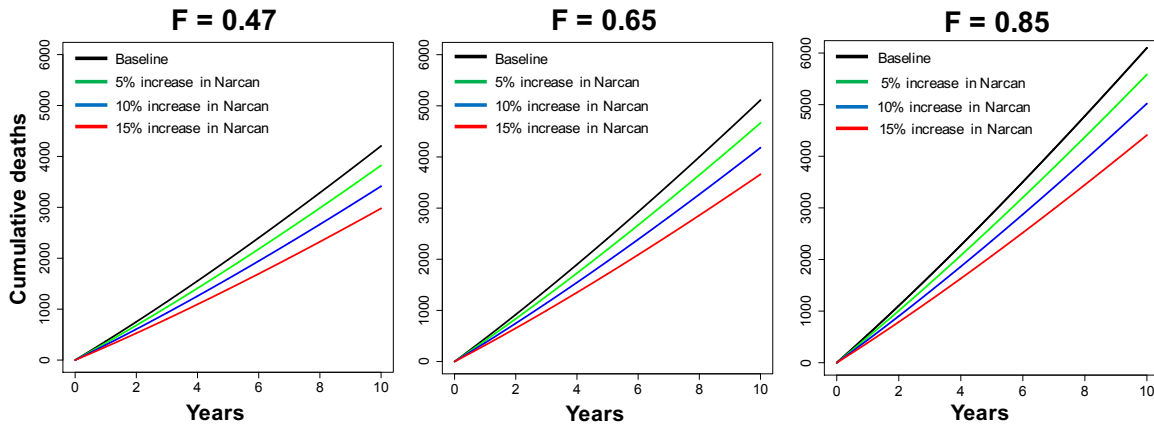


Figure 3: Graphs display the cumulative number of opioid overdose deaths for three different values of F (percentage of drugs containing fentanyl). In each plot, we assume Narcan is $n = 0.57$ (black), 0.62 (green), 0.67 (blue), and 0.72 (red).

5 Conclusions

In collaboration with the Allegheny County Department of Human Services, we developed a comprehensive mathematical model describing the opioid epidemic in Allegheny County. Two parameters, F and n , were included in the model to evaluate the effects that fentanyl and Narcan have on the crisis, particularly between 2014 - 2018. Results from model simulations indicate that increasing the distribution and availability of Narcan in the community will result in a meaningful reduction in the cumulative number of overdose deaths over a 10-year period; however, an increased presence of fentanyl will render Narcan less effective in reducing overdose deaths. Our model can be used by state and local policymakers, including Governor Wolf, or organizations, such as the Allegheny County DHS, to inform their decisions about the most beneficial way to allocate future funding to combat the opioid epidemic. Further investigation could enhance the model to determine if certain characteristics of the population—such as age, gender, social class, or culture—play a significant role in the opioid epidemic and influence the likelihood that an individual will become addicted or suffer from an overdose.

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